

REMARKS

Formal Matters

Claims 1-74, 76-84, 86 and 87 are pending in the present application. Claims 1-20, 25-44, and 50-65 have been withdrawn by the Examiner as directed to one or more non-elected inventions. Claims 21-24, 45-49, 66-74, 76-84, and 86-87 are pending for examination. Claims 21 and 45 are in independent form. No new matter has been added.

Applicants appreciate the Examiner's withdrawal of the objections to claims 68 and 78 in light of Applicants' January 14, 2009 Amendment and Response.

In view of the following remarks, Applicants respectfully request reconsideration of claims 21-24, 45-49, 66-74, 76-84, and 86-87, the claims presently under examination in the present application.

Claim Rejections- 35 U.S.C. § 102(a) and 102(e)

In the Action, the Examiner rejected Claims 21, 22, 24, 45, 46, 48, 49, 66-69, and 76-79 of the present application under 35 U.S.C. § 102(a) and 35 U.S.C. § 102(e) for alleged anticipation by Hennessy et al., US Pub. No. 2004/0016702 (herein "Hennessy"). Applicants respectfully traverse.

A. The Previously Submitted Rule 1.131 Declaration Is Sufficient to Overcome Hennessy.

In the prior response, dated January 14, 2009, Applicants submitted a declaration under 37 C.F.R. 1.131 for purposes of antedating Hennessy. In the Office Action, the Examiner asserted that the declaration is not sufficient to overcome Hennessy because "Applicant has not established that less than all of the named inventors invented the subject matter of the present claims, and therefore, a declaration signed by only one of the inventors is not sufficient to overcome the previously-made rejection" and because "the evidence submitted on January 14, 2009 only describes the synthesis of the particles and does not describe any methods for using them, particularly methods requiring their use in a mixture of oppositely charged ion exchange particles for the purification of PCR or DNA sequencing reaction products." [Office Action pp. 14-15]. Applicants respectfully traverse.

As a threshold issue, Applicants submit that the declaration could be considered atypical in comparison to Rule 131 declarations in general. The disclosure of Hennessy upon which the Examiner relies is directed to the use of a different type of size-exclusion ion-exchange particle than is described and claimed in the present application. Thus, the 131 declaration relates to (i) the differences in the particles of the present application and the particles of Hennessy, and (ii) the invention of the particles of the present application and their uses prior to the invention of the other type of particles and their uses as described in Hennessy.

As to the previously-filed declaration, the declarant, Dr. Aldrich N.K. Lau, stated expressly that he was an inventor on the Hennessy reference, that Hennessy relates to encapsulated particles as opposed to the polyelectrolyte coated particles of the present application, that the work he did on the Hennessy encapsulated particles and the present polyelectrolyte coated particles overlapped in time, and that “my work on reducing to practice various embodiments of the polyelectrolyte particles of the present application, especially as claimed in independent claims 21 and 45, was done before the filing of Hennessy ‘702.” [January 14, 2009 Declaration of Dr. Aldrich N. K. Lau Under 37 CFR 1.131 at ¶¶ 6-8]. Thus, Dr. Lau has plainly referenced the reduction to practice of the uses of the inventive polyelectrolyte particles of the present application that are recited in independent claims 21 and 45 of the present application. Moreover, in light of the uses to which Dr. Lau’s encapsulated particles were put in Hennessy (*e.g.*, “purification of polymerase chain reaction (PCR) products” and “purification of DNA sequencing reaction mixtures” [Hennessy, ¶ 28]), it is indisputable, in context, that in inventing the polyelectrolyte particles of the present application, Dr. Lau contemplated their use in methods for purifying PCR reaction products and purifying DNA sequencing reaction products as recited in claims 21 and 45.

For the avoidance of doubt, Applicants submit herewith a Supplemental Declaration of Aldrich N.K. Lau that addresses the foregoing issues. Applicants respectfully submit that the January 14, 2009 Declaration and the Supplemental Declaration submitted herewith establish that various embodiments of methods of the present application were invented prior to the effective date of Hennessy. Applicants further note that the scope of a Rule 131 declaration need not show any more than what the reference shows, MPEP 715.02, and Applicants have shown by the declarations that subject matter of claims 8 and 21 commensurate in scope with the subject matter of Hennessy relied upon by the Examiner was invented prior to the effective date of

Hennessy. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 102(a) and 35 U.S.C. § 102(e) over Hennessy be withdrawn.

B. Hennessy Does Not Anticipate Claims 21 and 45.

Without suggesting or admitting that Hennessy is “prior art” to the pending claims of the present application (indeed, Applicants aver that Hennessy is not prior art to the pending claims of the present application) and without waiving their right to submit additional evidence and argument regarding the date of invention for each of the pending claims, and solely to expedite prosecution, Applicants respectfully submit that Hennessy fails to teach all of the features of pending claims 21 and 45.

Claims 21 and 45 each recites “an ion exchange core coated by exposing the core to a polyelectrolyte copolymer material.” Hennessy does not teach at least that feature of claims 21 and 45. Instead, the size-exclusion ion-exchange particles in Hennessy are formed by microencapsulating an ion exchange core by exposure of the ion-exchange core to unpolymerized monomers and then polymerizing them in place on, in, and around the ion-exchange core, to form a size-exclusion polymer shell. Exposure of an ion-exchange core to individual monomers (as in Hennessy) is not the same as exposing an ion-exchange core to an already-formed size-exclusion polymer (as in the present application). Indeed, Hennessy is fundamentally different because a size-exclusion resin that is micro-encapsulated (*i.e.*, polymerized in place) on, in, and around an ion-exchange core forms a shell around the ion-exchange core, whereas a coating of ionic polyelectrolyte polymers, as in the present application, adheres by ionic bonding of the polymers to the ion-exchange core.

As Dr. Lau explained in his previously submitted Rule 131 declaration, a size exclusion shell encapsulates the particles in Hennessy, which he invented. In contrast, Dr. Lau explains that the particles in the present application, which he also invented, are coated with an ionic polyelectrolyte. [January 14, 2009 Declaration of Dr. Aldrich N. K. Lau Under 37 CFR 1.131 at ¶¶ 6-8]. The distinction drawn by Dr. Lau is reflected and confirmed in the present specification and in Hennessy.

(i) *Polyelectrolyte-Coated Particles of the Present Application.*

In the present specification, the polyelectrolyte particles are described as formed of an ion exchange core that is coated with pre-fabricated polyelectrolyte polymers, including by exposure of the ion exchange core to an excess of polyelectrolyte, exposure of the ion exchange core to a polyelectrolyte containing charges opposite to that of the core, and alternating exposures to polyelectrolyte material of opposite charges to build up multiple layers of alternative polyanion and polycation. [See, e.g., Specification ¶¶ 29-30 and 34-35]. The examples discuss using pre-formed polyelectrolyte polymer material to coat ion exchange core material. [Specification ¶¶ 70-71 and 72-75 (e.g., “poly(AA-co-DMA)polyelectrolyte” formed prior to coating by free radical polymerization)].

(ii) *Micro-Encapsulated Particles of Hennessy.*

In contrast to the polyelectrolyte-coated particles of the present application, Hennessy forms encapsulated particles by polymerizing monomer *in-situ* on, in, and around the ion exchange core. Hennessy explains that the size-exclusion ion-exchange particles therein have “an ion-exchange core micro-encapsulated by a shell capable of size exclusion.” [Hennessy ¶25]. Hennessy describes the microencapsulation of the ion exchange core as follows:

The terms “micro-encapsulation,” “micro-encapsulated,” or the like, refer to a process of encapsulation on the individual particle level. In one embodiment, a core of liquid, solid, and/or gas is micro-encapsulated with a shell to control access to the core. In various other embodiments, micro-encapsulation can coat the entire exterior surface of the core (and optionally interior surfaces), or it can coat only a portion of the exterior surface of the core (and optionally interior surfaces).

[Hennessy ¶25]. Hennessy also cross-references and incorporates by reference a concurrently-filed U.S. patent application to Lau et al. entitled “Size-Exclusion Ion Exchange Particles,” and cites “Attorney Docket No. 4885” in lieu of an application serial number which had not yet been assigned. Applicants respectfully submit that the referenced concurrently-filed application is Application Serial Number 10/414,179 to Lau et al. (herein “Lau ‘179”), which published the same day as Hennessy as U.S. Patent Publication No. 2004/0018559.¹

¹ The filing date referenced on the face of Hennessy appears to be incorrect; according to records available on public PAIR, the correct filing date for Hennessy is April 13, 2003, the same filing as the Lau et al. application referenced in the text.

Hennessy, via the incorporation of Lau '179, further describes the microencapsulation process, and explains that the size-exclusion shell is formed by *in-situ* polymerization:

[A] shell can be formed simultaneously with micro-encapsulation of the ion-exchange core. For example, a shell can be formed by inverse emulsion polymerization of a water-soluble reactive monomer, for example, acrylamide, to form a hydrogel. As shown in FIG. 3, an ion-exchange core 10 can be placed in an aqueous monomer solution in a vessel 40. The ion-exchange core 10 can be a surface-activated ion-exchange core. The aqueous monomer solution can include, for example, one or more monomer, for example, acrylamide or N-vinylpyrrolidone, a cross-linker, for example, 2,2-bis(acrylamido)acetic acid, and/or a free radical initiator, for example, sodium persulfate, potassium persulfate, or an azo compound. The solution can further include one or more of a catalyst, a terminator, a chain-stopper, a chain-transfer agent, a promoter, a buffer, and an accelerator.

Next, an oil phase 42 can be added to the vessel 40. The oil phase 42 can include an oil and a surfactant, or an oil including a surfactant. An exemplary oil phase 42 is Petroleum Special (available from Fluka, Buchs SG, Switzerland) and includes a surfactant having a low Hydrophilic Lyophilic Balance (HLB) value, for example, sorbitan monooleate (HLB=4.3). The vessel contents can be subjected to inverse emulsification and polymerization, resulting in the formation of size-exclusion ion-exchange particles 30 having an ion-exchange core 10 micro-encapsulated by a partially cross-linked size-exclusion shell 20 in an aqueous solution 46 in vessel 40. SEIE particles produced by inverse emulsion polymerization can be spherical or nearly spherical in shape, or other shapes depending upon of the shape of the ion-exchange core.

According to various embodiments, a shell can be formed by passing a heated ion-exchange core that is impregnated with an initiator, a catalyst, or both, through a fluidized bed of one or more reactive monomers suitable for forming a shell. The fluidized bed can include, for example, acrylamide and N,N'-methylenebisacrylamide. The monomers and/or polymers in the fluidized bed can be in powder form and can be flowed and/or melted into and onto the ion-exchange core. SEIE particles produced by a fluidized bed reaction can be irregular in shape.

Further, the application serial numbers for Hennessy (10/413,797) and Lau '179 (10/414,179) indicate that the two applications were filed concurrently.

[Hennessy ¶1 (Lau '179 ¶¶ 43-45 (emphasis added))]. Thus, the size-exclusion shell of Hennessy is formed *in-situ* by polymerization of a monomer in aqueous solution through an inverse emulsification process (or through a fluidized bed process wherein the ion-exchange core is impregnated with an initiator, a catalyst, or both). Further, Hennessy's example of making the size-exclusion shell makes clear that the shells are not formed by exposing ion-exchange cores to pre-formed polyelectrolyte polymer:

A solution was prepared from 2.4957 g (35.11 mmol) acrylamide (99+% pure, Aldrich Chemical, St. Louis, Missouri) and 0.7021 g (4.55 mmol) of N,N'-methylenebisacrylamide (99+pure, Aldrich Chemical) in 11.9391 g of water (Milli-Q Water System, Millipore of Billerica, Massachusetts). To the solution was added, with swirling, a suspension of 0.7158 g of MACRO-PREP HQ macroporous anion-exchange core (Bio-Rad of Hercules, California) in 2.0075 g of water (Milli-Q Water System, Millipore). The suspension of MACRO-PREP HQ was prepared 30 minutes ahead of time with occasional swirling prior to use. The mixture of monomer solution and the MACRO-PREP suspension was poured into a solution of 1.0072 g of SPAN-80 (sorbitan monooleate, Fluka of Buchs, Switzerland) in 20.10 g of PETROLEUM SPECIAL (bp 180-220.degree. C., Fluka) and stirred at 3600 rpm. Emulsification was carried out at ambient temperature for 2.5 minutes. The emulsion was added to a 24/40 three-necked round bottom flask, equipped with a water-cooled condenser, a bleeding tube for purging, and a mechanical stirrer with a 1" stainless steel 3-blade propeller. At a stirring speed of 100 rpm, the emulsion was purged by ultra-pure helium at a flow rate of 100 mL/min for 30 minutes. At the beginning of purging, 0.5 mL (0.044 mmol) of a solution of 0.4507 g of ammonium persulfate (99.99+% pure, Aldrich Chemical) in 22.1652 g of water (Milli-Q Water System, Millipore) was added. At the end of purging, the reaction flask was lowered into an oil bath at 45±1°C and 50 µL (0.33 mmol) N,N,N'-tetramethylenethylene-diamine was added to the reaction flask. Polymerization was conducted at 45±1°C for 5.5 hours.

[Hennessy ¶1 (Lau '179 ¶80 (emphasis added))]. By requiring the use of a cross-linker and/or initiator, Hennessy emphasizes the point that the size-exclusion resin is polymerized in place on, in, and around an ion-exchange core to form a physical shell around the ion-exchange core.

By exposing the ion-exchange core to individual monomers, rather than much larger pre-fabricated polyelectrolyte polymers, the shell material in Hennessy penetrates into the crevices

and pores of the ion-exchange material of the core, allowing for coating of the interior surfaces of the ion-exchange core as well as the exterior surfaces. As explained in Hennessy:

The shell material can at least partially fill one or more pore or surface feature, for example, pores, cracks, crevices, pits, channels, holes, recesses, or grooves, of the ion-exchange core. For example, an ion-exchange core can be coated on all internal and external surfaces with a monomer suitable for forming a shell. The monomer can be reacted with one or more of a second monomer, a catalyst, or an initiator to form a cross-linked size-exclusion polymer on all surfaces of the ion-exchange core, with the outermost surface of the size-exclusion polymer forming the outermost surface of the size-excluding shell.

[Hennessy ¶1 (Lau '179 ¶48)].

(iii) *Hennessy Does Not Teach “an ion exchange core coated by exposing the core to a polyelectrolyte copolymer material” As Recited In Claims 21 and 45.*

The aforementioned feature of the claim, “an ion exchange core coated by exposing the core to a polyelectrolyte copolymer material,” distinguishes the particles of the present claims from the particles in Hennessy. For example, by stating that the ion exchange core is exposed to a polyelectrolyte copolymer material, the claim language indicates that the polyelectrolyte copolymer material is already in existence (*i.e.*, polymerized) and is not formed or polymerized *in-situ* on, in, and around the ion exchange core.

* * *

For at least these reasons, Hennessy is not prior art to the pending claims and, assuming for argument that Hennessy were to be considered prior art under 35 U.S.C. 102 despite Applicants' argument and declarations, it nevertheless fails to teach at least the “ion exchange core coated by exposing the core to a polyelectrolyte copolymer material” feature of claims 21 and 45. Hennessy therefore does not anticipate either claim 21 or claim 45. Because claims 22, 24, 46, 48, 49, 66-69, and 76-79 each depends, directly or indirectly, from claim 21 or claim 45, those claims are not anticipated by Hennessy for at least the same reasons that claims 21 and 45 are not anticipated. Withdrawal of the rejections of claims 21, 22, 24, 45, 46, 48, 49, 66-69, and 76-79 of the present application under 35 U.S.C. § 102(a) and 35 U.S.C. § 102(e) for alleged anticipation by Hennessy is therefore respectfully requested.

Claim Rejections- 35 U.S.C. § 103(a)

A. Claims 23, 47, 70-72, 80-82, 86, and 87 Are Not Obvious Over Hennessy.

In the Action, the Examiner rejected claims 23, 47, 70-72, 80-82, 86, and 87 under 35 U.S.C. §103(a) as unpatentable over Hennessy. Applicants respectfully traverse.

As discussed above, Hennessy is not prior art to the pending claims and, assuming for argument that Hennessy was an appropriate reference under 35 U.S.C. 102 and available as a reference under 35 U.S.C. 103, it nevertheless fails to teach at least the “ion exchange core coated by exposing the core to a polyelectrolyte copolymer material” feature of independent claims 21 and 45. Claims 23, 47, 70-72, 80-82, 86, and 87 each depends from either claim 21 or claim 45, and therefore includes the “ion exchange core coated by exposing the core to a polyelectrolyte copolymer material” feature.

Applicants respectfully submit that nothing in Hennessy suggests the use of an ion exchange core coated by exposing the core to a polyelectrolyte copolymer material. As discussed above, Hennessy’s particles are formed by exposing ion-exchange cores to individual monomers and polymerizing those monomers *in-situ* on, in, and around the ion-exchange core material to form a physical shell around the ion-exchange core. Applicants respectfully submit that nothing in Hennessy teaches or suggests particles in which a size-exclusion shell is formed by exposing an ion-exchange core to a pre-formed polyelectrolyte copolymer material.

For at least these reasons, claims 23, 47, 70-72, 80-82, 86, and 87 are not rendered obvious by Hennessy. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of these claims as allegedly obvious over Hennessy.

B. Claims 73, 74, 83, and 84 Are Not Obvious Over Hennessy In View Of Breadmore.

In the Action, the Examiner rejected claims 73, 74, 83, and 84 under 35 U.S.C. §103(a) as unpatentable over Hennessy in view of Breadmore et al., WO 03/104774 (herein “Breadmore”). Applicants respectfully traverse.

As discussed above, Hennessy is not prior art to the pending claims and, assuming for argument that Hennessy was an appropriate reference under 35 U.S.C. 102 and available as a reference under 35 U.S.C. 103, it nevertheless fails to teach at least the “ion exchange core coated by exposing the core to a polyelectrolyte copolymer material” feature of independent

claims 21 and 45. Claims 73, 74, 83, and 84 each depends from either claim 21 or claim 45 and therefore includes the “ion exchange core coated by exposing the core to a polyelectrolyte copolymer material” feature.

Applicants respectfully submit that nothing in Hennessy teaches or suggests the use of an ion exchange core that is coated by exposing the core to a polyelectrolyte copolymer material. As discussed above, Hennessy’s particles are formed by exposing ion-exchange cores to individual monomers and polymerizing those monomers *in-situ* on, in, and around the ion-exchange core material to form a physical shell around the ion-exchange core. Applicants respectfully submit that nothing in Breadmore independently renders either claim 21 or claim 45 obvious or cures the deficiency of Hennessy.

For at least these reasons, claims 73, 74, 83, and 84 are not rendered obvious by Hennessy in view of Breadmore. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of these claims as allegedly obvious over Hennessy in view of Breadmore.

Provisional Non-Statutory Double Patenting Rejections

In the Office Action, claims 45, 80-82, and 87 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over claims 8, 21, and 29-36 of co-pending application 11/057,936 in view of Hennessey. Additionally, in the Action, claims 45, 80-82, and 87 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over claims 12, 15, 21, 22 and 28-35 of co-pending application 11/355,872 in view of Hennessey. [Office Action pp. 9-14].

The Examiner acknowledged Applicants’ argument, presented in the immediately preceding response (dated January 14, 2009), that the present application was filed before 11/057,936 and 11/355,872 and should therefore be issued without a terminal disclaimer, and that the Applicants will submit terminal disclaimers for the two co-pending applications, 11/057,936 and 11/355,872. However, the Examiner maintained the provisional non-statutory obviousness-type double patenting rejection pursuant to MPEP §804 because, in the Examiner’s view, the present application was not in condition for allowance. [Office Action p. 17].

Applicants respectfully submit that in light of the remarks provided herein, the present application is now in condition for allowance. As provided in MPEP § 804 B1, paragraph 3, the

Applicants have submitted terminal disclaimers for the two co-pending applications, 11/057,936 and 11/355,872. Accordingly, Applicants respectfully request withdrawal of the provisional non-statutory obviousness-type double patenting rejection and allowance of all pending claims of the present application.

Response to Examiner's Comments

In the Office Action, the Examiner made assertions regarding a secondary reference, Breadmore. [Office Action pp. 7-9]. Applicant believes that response to those assertions is unnecessary because the assertions are no longer relevant to the pending claims and are moot in light of the remarks contained herein and the removal of Hennessy as a reference under 37 CFR §1.131. Applicant further believes that this is nevertheless a complete response to the Office Action because Applicants have addressed each ground for objection and rejection set forth in the Office Action.

Applicants' decision to decline to specifically address certain assertions in the Office Action which Applicant believes have become moot and of no further relevance is not, and should not be interpreted as, acquiescence in or agreement with the positions asserted in the Office Action.

Conclusion

In view of the above remarks, reconsideration of the rejections and allowance of each of claims 21-24, 45-49, 66-74, 76-84, and 86-87 in connection with the present application is earnestly solicited.

If the Examiner finds that a telephone conference would expedite the prosecution of this case, the Examiner is invited to contact me at the telephone number listed below.

Fee Authorization

A three-month extension of time is hereby requested. The Commissioner is hereby authorized to charge **Deposit Account No. 50-3994 (order no. 5118 US)**. Any deficiency or overpayment should be charged or credited to this deposit account.

Respectfully submitted,

Date: September 30, 2009

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